REMARKS/ARGUMENTS

1. Remarks on the amendment

Claim 11 has been amended to more specifically define Applicant's claimed invention. Antecedent basis of the amendment of Claim 1 can be found page 20, lines 20-25, and page 24, lines 5-7 of the Specification as filed.

Applicant submits no new matter is introduced by the amendment.

2. Response to the Rejection under 35 USC §103(a)

Claims 11-16 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Pearlman et al. (WO/9918800). This rejection is respectfully traversed.

Applicant submits that nothing in the art of record teaches or suggests the subject matter defined by the amended independent Claim 11.

More specifically, as positively recited in the amended independent Claim 11, the instant dermatological composition for topically treating dermatological conditions comprising transient acantholytic dermatitis, acne miliaris necrotica, acne varioliformis, perioral dermatitis, acneiform eruptions, acne vulgaris, or seborrheic dermatitis, said composition consisting of an avermectin compound in a concentration from 0.05% to 0.1% (w/v) in a lotion consisting of glycerin, hydrogenated polyisobutene, cetearyl alcohol, polyoxyethylene ether of cetyl and stearyl alcohol, macadamia nut oil, dimethicone, tocopheryl acetate, stearoxytrimethylsilane, stearyl alcohol, panthenol, farnesol, benzyl alcohol, phenoxyethanol, acrylates/C10-30 alkyl acrylate crosspolymer, sodium hydroxide, citric acid, and water; said composition not causing skin irritation of patients suffering from said dermatological conditions upon repetitive daily use.

As defined, the instant composition is free of chemical components that may cause skin irritation, such as parabens, sodium lauryl sulfate, and quaternium 15. Moreover, as a composite of its chemical components, inclusive both active ingredient and the medium, the instant composition possesses a property of not causing skin

irritation upon repetitive daily use. This is particularly required with those suffering from the defined dermatological conditions, whose skin is more sensitive due to the clinical conditions.

In the instant Office Action, the Examiner states that Pearlman et al. does not explicitly disclose Cetaphil® moisturizing lotion as the pediculocide or explicitly disclose the concentration of ivermectin from about 0.05 to about 0.1% or 0.075%; however, it would have been obvious to one skilled in the art to substitute the Cetaphil® moisturizing lotion for the Cetaphil® Cleanser as both products are produced by the same laboratories and Pearlman et al. teaches of the use of cleansers and lotions/moisturizers interchangeably as a pediculostatic agent.

Moreover, the Examiner further states that it would have been obvious to one skilled in the art to include an active agent (i.e., ivermectin) in a concentration from about 0.1%, etc. in combination with Cetaphil® Cleanser or Cetaphil® moisturizing lotion, as Pearlman et al. teaches of the concentration of typically from about 0.25% to about 2.5% where the concentration of typically from about 0.25% of Pearlman et al. encompasses the concentration of from about 0.1% and from about 0.075%, as the higher and lower limits of the range of about 0.1% is not defined.

Applicant strongly disagrees for the following reasons.

First, Claim 11 has been amended to more specifically define the concentration of avermectin compound in the claimed composition. As such, the issues raised by the Examiner on the higher and lower limits are moot.

Second, Applicant maintains that Pearlman et al.'s opposite teaching does not render the composition and the technical advantages of the presently claimed invention obvious.

As disclosed in the present application, the instant composition contains a very low effective concentration of the active component, namely from 0.05% to 0.1% (w/v) of an avermectin compound. As demonstrated extensively by examples, at this very low concentration of the active component the instant composition is clinically effective in

treating transient acantholytic dermatitis, acne miliaris necrotica, acne varioliformis, perioral dermatitis, acneiform eruptions, acne vulgaris, or seborrheic dermatit, and at the same time it does not cause side effect and can be used for daily treatment for extended period of time. On the other hand, the medium of the instant composition is particularly suitable for topical treatment of the defined conditions. Cetaphil® moisturizing lotion is non-comedogenic and does not contain fragrance, lanolins or parabens that are known cause skin irritation.

It is important to understand that the subject dermatological conditions require repetitive exposure of the affected skin with the topical composition for extended period of time. As such, if any components or combinations thereof in the composition cause undesired reaction of the skin during the treatment, the topical treatment would not be successful. Therefore, the chemical composition as a whole is required possessing the property of not causing skin irritation of patients suffering from said dermatological conditions upon repetitive daily use.

The present inventor has discovered through clinical trials that the combination of very low concentration of ivermectin with the specific medium as defined is particularly effective for treating the subject conditions. After daily use of the instant composition for up to several months no skin irritation, or increase of skin sensitivity was found (Examples 4-14). As shown in many examples the instant composition was applied at bed time to ensure overnight exposure of the affected area to the composition. As further disclosed, the instant composition can be applied to very sensitive areas, such as around the eyes or directly on the eyelids without causing irritation, and can be used to effectively treat perioral dermatitis that affect these sensitive areas.

On the contrary, Pearlman et al's teaching is directed to a pediculostatic agent used in elimination of head lice with a limited time of skin contact, in which the considerations on the properties of the composition and their suitability in treating those suffering from the dermatological conditions as defined in Claim 11 are completely absent. This can be evidenced by Pearlman et al's following teachings.

Pearlman et al teach that commercially available products such as soaps, cleansers, lotions, moisturizers, conditioners and shampoos may be used as

pediculostatic agent (page 17, lines 1-5). Pearlman et al further teach that the pediculostatic agent includes commercially available skin cleansers, skin conditioners, personal lubricating jelly, sunscreen, mouthwash, toothpaste, and other products; and the pediculostatic agent also includes commonly available honey, vinegar, mustard, gelatin, yogurt, or other foodstuffs, which may be applied for a period of time sufficient to stun the lice (page 17, lines 11-20).

In the preferred embodiments, Pearlman et al teach BABY MAGIC® baby shampoo, SUAVE® Baby Care bath soap and CETAPHIL® Cleanser (page 17, line 22 to page 18, line15). All of these products contain chemical components, such as sodium lauryl sulfate, quaternium 15, parabens and fragrance, known to cause skin irritation or contact dermatitis. With regard to the most preferred embodiment of Pearlman et al, CETAPHIL® Cleanser, this product contains three parabens, methyl paraben, propylparaben and butylparaben, which are known causing skin irritation. These chemical components render Pearlman et al's compositions not suitable for prolonged skin exposure and not suitable for topical treatment for those suffering from the dermatological conditions as defined in the presently claimed invention.

Therefore, Pearlman et al's teaching of compositions containing multiple chemicals that are known causing skin irritation teaches away from the instant composition that requires free of these chemicals and requires not causing skin irritation upon repetitive daily use.

In this regard, the Examiner states that the instant claims are not drawn to the method of administering the composition for treating the subject condition, or for prolonged skin exposure. Applicant points out that the Examiner's rationale is flawed. The instant composition requires free of numerous chemicals taught and deemed appropriate by Pearlman et al, and further requires a property of not causing skin irritation upon repetitive daily use. These are structural limitations of the claimed composition, not limitations to a method step. As readily understood by those having ordinary skill in the art, the properties of a composition are determined by chemical components comprised in the composition and their combined effect. Therefore, it is improper for the Examiner to disregard the structural limitations of the claimed

composition, and deem Pearlman et al's lack of teaching or recognition of the required properties as irrelevant.

Third, with regard to ivermectin, Pearlman et al. specifically teach that the pediculocidal active ingredients can be used at levels effective to achieve their intended results, namely killing head lice, which are at a concentration from about 0.25% to about 2.5% (see page 6, third paragraph). Therefore, contrary to the instant composition, Pearlman et al's method requires a substantially higher ivermectin concentration in order to be effective to treat head lice infestations. It should be particularly pointed out that the lowest ivermectin concentration of about 0.25% in Pearlman et al. is more than double of the highest concentration in the instant composition. Therefore, Pearlman et al clearly teaches away from the presently claimed invention.

In the Office Action, the Examiner emphasizes the phrase "typically from about 0.25% to about 2.5%" disclosed by Pearlman et al. However, put into context, Pearlman et al. expressly teach the concentration of the pediculocidal active ingredients is at levels effective to achieve their intended results, which is killing the head lice. Pearlman et al. does not teach that a concentration less than 0.25% can be effective in killing head lice. Based on Pearlman et al's teaching, one skilled in the art would not reduce the concentration of the pediculocides, if one wants to preserve the effectiveness of the composition for killing the head lice.

Moreover, it is apparent that Pearlman et al do not recognize the desire and advantages of using a very low concentration of ivermectin to avoid clinical side effects in treating those suffering from the dermatological conditions defined in the instant application. From the above, it is evident that Pearlman et al's teaching is only pertinent to a composition having a pediculostatic or pediculocidal property.

Fourth, the Examiner states that Pearlman et al. teach the topical composition comprising a pediculocide (i.e., ivermectin) with a pediculostatic agent (i.e., CETAPHIL® Cleanser) and further teaches that any commercially available product, such as those that are non-toxic, may be used as the prediculostatic agent, not excluding CETAPHIL®

moisturizing lotion. Therefore, the Examiner maintains that it would have been obvious to one skilled in the art to substitute the CETAPHIL® moisturizing lotion for the CETAPHIL® Cleanser as both products are produced by the same company (Galderma Laboratories, Inc.) (paragraph 15 of the Office Action).

Applicant points out that according to Pearlman et al's teaching, soaps, cleansers, lotions, moisturizers, conditioners, shampoos, personal lubricating jelly, sunscreen, mouthwash, toothpaste, honey, vinegar, mustard, gelatin, yogurt, or other food-stuffs are all suitable as pediculostatic agent. This disclosure includes endless commercial personal care and food products. Using the Examiner's rationale, all of these can be used non-toxic interchangeably as pediculostatic agent to stun the lice. However, this is a different field from clinical treatment of dermatological conditions. That which is deemed appropriate, non-toxic, and interchangeable in head lice treatment does not reflect or satisfy their suitability in treating the defined dermatological conditions.

For example, sodium lauryl sulfate is an anionic surfactant commonly used in baby shampoos, and deemed non-toxic for external use. However, in dermatology it is well known sodium lauryl sulfate causes skin irritation and therefore, it is not suitable to be used in the topical composition for treatment of the defined clinical conditions. In another example, methyl paraben, propylparaben and butylparaben are effective antimicrobials commonly used in shampoo and cleanser products, and deemed non-toxic for external use. However, as discussed above, parabens cause skin irritation and are not suitable in the instant composition used in treating the defined dermatological conditions.

Based on Pearlman et al's teaching of effective pediculostatic agents for stunning the lice, one skilled in the art would not be able to obtain, without undue experimentations, the instant composition that does not cause skin irritation of patients suffering from the defined dermatological conditions upon repetitive daily use. As discussed above, the skin of the patients suffering from the defined dermatological conditions is more sensitive. Without actual clinical trial, one would not be able to determine the properties of the topical composition.

On the other hand, Galderma Laboratories, Inc. produces hundreds of different

commercial products, and each of them has its own composition, property and utility. Therefore, it is not obvious for one skilled in the art to substitute one product for another simply because the two products are made by the same company.

In *Syntex (USA) LLC vs. Apotex, Inc.*, 407 F.3d 1381 (Fed. Cir. 2005), the court has made it clear that "the bare question of whether it would have been obvious to substitute one surfactant for another misplaces the proper focus on the obviousness of the invention as a whole, and likely invites hindsight conclusion, forbidden by our precedent".

In the Office Action the Examiner specifically picks and chooses honey and yogurt from Pearlman et al's laundry list as examples of not containing paraben, while disregards the facts that all preferred embodiments of the reference contain one or more chemicals that are known causing skin irritation. Applicant submits that the Examiner cannot pick and choose from a reference only what is need to support a given position to the exclusion of other parts necessary to appreciate what the reference suggests, *In re Inland Steel*, 265 F. 3d 1354, 60 U.S.P.Q.2d 1396 (Fed. Cir. 2001).

Fifth, the Examiner states that the intended use of the dermatological composition is not afforded any patentable weight, and "The recitation of a new intended use for an old product does not make a claim to that old product patentable." *In re Schreiber*, 44 USPQ2d 1429(Fed. Cir. 1997). As submitted previously, this is an improper application of the case law. The instant composition is structurally different from Pearlman et al's cleanser and ivermectin combination, and the concentration of avermectin compound in the presently claimed composition is different from that in Pearlman et al. Therefore, the instant composition is not an old product.

Moreover, as discussed above, in addition to exclusion of the chemicals that cause skin irritation, the requirement of "not causing skin irritation of those suffering from the subject dermatological conditions upon repetitive daily use" is a further structural limitation defining the property of the claimed composition, which is determined by the individual components used in the composition and their combined effect. Therefore, it is improper for the Examiner to construe the property of the composition merely as an

intended use.

Sixth, the Examiner's construction of the concentration range of the active component of the reference is improper. The Examiner relies on Titanium Metals Corp. of America vs. Banner, 778 F. 2d 775, 227 USPQ 773 (Fed. Cir. 1985), in which the Court held as proper a rejection of a claim directed to an alloy of "having 0.8% nickel, 0.3% molybdenum, up to 0.1% iron, balance titanium" as obvious over a reference disclosing alloys of 0.75% nickel, 0.25% molybdenum, balance titanium and 0.94% nickel, 0.31% molybdenum, balance titanium.

As discussed previously, in Titanium Metals Corp of America vs. Banner, the claimed 0.8% nickel is between 0.75% and 0.9% shown by the reference, and the difference of the claimed nickel from the reference is 6% and 12.5%, respectively. As to the molybdenum, the claimed 0.3% molybdenum is also between 0.25% and 0.31% of molybdenum shown by the reference, and the difference of the claimed molybdenum from the reference is 15% and 3%, respectively. As to titanium, the claimed titanium is 98.8% which is between 99% and 98.75% shown by the reference, and the difference of the claimed titanium from the reference is 2% and 0.05%, respectively.

This is substantially different from the present case. In the present case, the concentration of the ivermectin is outside the range of Pearlman et al's composition, and the lowest ivermectin concentration of about 0.25% in Pearlman et al. is more than double of the highest concentration in the instant composition. More specifically, the lowest concentration of 0.25% in Pearlman et al. is 150% higher than the highest concentration of 0.1% in the instant composition. Therefore, it is improper to construe that "0.1%" would overlap with a concentration that is 150% higher; and it is improper to construe a concentration of "about 0.25%" would encompass a concentration that is less than its 50%.

Furthermore, Pearlman et al also lack of teaching of other components of the instant composition. In order to apply Titanium Metals Corp of America vs. Banner, one has to address first whether Pearlman et al teach a combination of ivermectin with the specific components of Applicant's claimed composition defined in Claim 1 and a

composition possessing the required property. This has been discussed above and has been shown that Pearlman et al fail to provide a fair teaching in both aspects.

Therefore, Applicant maintains that Applicant's claimed dermatological composition defined in the amended Claim 11 is unobvious in view of the prior art of record.

With regard to Claims 12-16, these claims are dependent upon independent Claim 11. Under the principles of 35 U.S.C. §112, 4th paragraph, all of the limitations of each independent claim are recited in its respective dependent claims. As described above, independent Claim 11 is not obvious, as such Claims 12-16 are submitted as being allowable over the art of record.

Accordingly, Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. §103(a).

It is respectfully submitted that Claims 11-16, the pending claims, are now in condition for allowance and such action is respectfully requested.

Applicant's Agent respectfully requests direct telephone communication from the Examiner with a view toward any further action deemed necessary to place the application in final condition for allowance.

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Date of Signature

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